REMARKS

Claims 1-21 are pending.

Claims 15-21 have been withdrawn from consideration as being drawn to a non-elected invention.

Claim 1 has been amended. Support for the amendment is found, for example, at page 6, paragraph 4.

Claims 4, 12, and 13 have been amended for clarity. Consideration of the current amendment and the remarks that follow is respectfully requested.

Therefore, Claims 1 through 14 are currently pending.

No new subject matter has been added.

The amendment of claims in being done solely to expedite the prosecution of the application and an inference should not be inferred that the scope of the claims has been diminished in any respect. Applicant reserves the right to prosecute the original claims in this or a related application.

Specification Objection

The disclosure was objected to because of informalities. The disclosure contains multiple embedded hyperlinks and/or other form of browser-executable code.

Pages 4, 5, 32, 41, 43, 44, 49, 50, 54, 55, 57 and 58 have been amended to remove the language, thereby obviating the basis for this objection.

Reconsideration and withdrawal of the objection is respectfully requested.

Information Disclosure Statement Objection

The two Japanese references have not been considered by the Examiner.

A new information disclosure statement listing the Japanese references with English abstracts is attached herewith.

Applicant points out that English translations of the abstracts from these Japanese references were furnished with the references in the original Information Disclosure Statement.

Double Patenting Rejection under 35 U.S.C. §101

Claims 1-14 stand provisionally rejected under 35 U.S.C. §101 as claiming the same invention as that set out by claims 1-5 and 7-11 of copending Application No. 10/546,139, the national phase entry of PCT application PCT/FR04/00354, which corresponds to the present application. Applicant awaits a first Office Action in Application No. 10/546,139 and accordingly requests that the provisional rejection in the present case be held in abeyance.

NonStatutory Double Patenting Rejection

Claims 1 and 6 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 6 of copending Application No. 10/546,139. Applicant requests that this provisional rejection be held in abeyance until the presently claimed subject matter or that claimed in the copending application is deemed otherwise patentable.

Rejections under 35 U.S.C. § 112.

Claims 1-14 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for reciting "evolved microorganism", "permitting a modification", "cause it to evolve", and "evolution" in claim 1, and "production microorganisms" in claim 14. Further, dependent claims 9 and 13 stand rejected as allegedly indefinite for reciting an additional method step whereas it is asserted that the parent claims do not recite method steps. Applicant respectfully traverses.

Preliminarily, claim 1 has been amended to delete the phrases "permitting a modification", "cause it to evolve", and "to allow such evolution".

The essential inquiry with respect to 35 U.S.C. §112, second paragraph, is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity from the point of view of one possessing an ordinary level of skill in the pertinent art at the time the invention was made. Further, the definiteness of claim language must be analyzed in light of the content of the application (M.P.E.P. §2173.02).

Applicant notes that at page 3, paragraph 3, provides that the meaning of "evolved microorganism" is clearly defined.

Further, the specification clearly describes to one of reasonable skill in the art the meaning of "production microorganism" (see, for example, page 6, paragraph 3, and page 10, paragraph 2).

Regarding claims 9 and 13, Applicant points out that the claims depend from claims 8 and 12, respectively, which in turn depend from claim 1. Claim 1 recites three steps, a, b, and c. Applicant submits that the recital of additional step d in claims 9 and 13 is proper, and respectfully requests withdrawal of the rejections.

As supported by the exemplary excerpts cited above, Applicant submits that the claims as currently amended set out and circumscribe the present subject matter with a reasonable degree of clarity and particularity in view of the specification such that the skilled artisan can readily determine the full scope of the claimed subject matter. Accordingly, Applicant respectfully requests withdrawal of the rejection and allowance of claims 1-14.

Claim Rejections Under 35 U.S.C. §102

Claims 1-4 and 8-14 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Nakamori *et al.*, Appl. Micro. Biotech., 52:179-185, 1999 (Nakamori). Applicant respectfully traverses the rejection.

Claims 1-7 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by WO 93/177112. Applicant respectfully traverses the rejection.

Nakamori

Nakamori reports on bacteria subjected to treatment with a mutagen, followed by selection of desired mutant bacteria using a medium containing methionine analogues. The mutations introduced into bacteria by the method of Nakamori are random rather than pathway- or gene-specific, owing to the use of mutagen, and initially generate a wide variety of mutant bacterial genotypes.

In contrast, claim 1 and dependent claims 2-4 and 8-14 of the instant application are drawn to methods for preparing an evolved microorganism, which involve a first step of producing a modified microorganism by introducing a predetermined genetic alteration, particularly a gene modification that inhibits a metabolic pathway and thereby impairs the ability of the microorganism to grow. For technical clarity, claim 1 has been currently amended to recite that the genetic modification is a "directed" genetic modification. Support for the amendment is found, for example, at page 6, paragraph 4 of the specification.

Applicant submits that Nakamori does not describe the production of modified microorganisms by directed genetic modification, *i.e.*, introduction of predetermined genetic modifications. Accordingly, Applicant submits that Nakamori does not anticipate the currently claimed subject matter.

Further, while in Nakamori's method it is the random mutation in response to mutagen that generates a mutant having the desired phenotype and underlying genotype among a wide variety of mutants, the first step of genetic modification in the present claimed methods does not generate a microorganism having the final desired phenotype and genotype – rather, genetic

modification in the present methods sets the stage for evolution to achieve a genotype (critically including an evolved gene) that exhibits the desired phenotype in a subsequent step. In particular, given the metabolic defect achieved by directed genetic modification in the first step of the presently claimed methods, evolved microorganisms having desired metabolic properties are then selected for in a subsequent step by the application of selective pressure through the use of appropriate media. Applicant submits that Nakamori does not anticipate the instant claimed methods on this additional basis, and respectfully requests withdrawal of the rejections and allowance of the claims.

WO 93/177112

WO 93/177112 describes methods for enhancing methionine production in a fermentation process by transforming a microorganism with a homoserine-activating enzyme gene and a sulfur incorporating enzyme gene. The purpose of these modifications is to improve the production of methionine by over-expressing genes coding for enzymes involved in the biosynthesis pathway.

WO 93/177112 does not disclose inhibiting a metabolic pathway by genetic modification to impair the ability of the microorganism to grow, thereby providing for the application of selective pressure in respect of a particular metabolic pathway on evolving, descendant microorganisms with the use of appropriate media. Quite to the contrary, WO 93/177112 teaches methods for improving a desired biosynthesis pathway in a given microorganism by making particular genetic modifications that directly effect the biosynthesis improvement.

Accordingly, Applicant submits that WO 93/177112 does not anticipate the presently claimed subject matter and respectfully requests that the rejections be withdrawn and the claims allowed.

CONCLUSION

In view of the above, Applicant respectfully submits that the present application is in condition for allowance. Reconsideration of the present application and a favorable response are respectfully requested.

This response is being submitted on or before May 18, 2007, with the required fee of $300 for a one-month extension of time and the Supplemental Information Disclosure Statement fee, making this a timely response. It is believe that no additional fees are due in connection with this filing. However, the Commissioner is authorized to charge any additional fees, including extension fees or other relief which may be required, or credit any overpayment and notify us of same, to Deposit Account No. 04-1420.

Respectfully submitted,

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